

# THE LANCET **Neurology**

## **Supplementary webappendix**

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Barger LK, Flynn-Evans EE, Kubey A, et al. Prevalence of sleep deficiency and use of hypnotic drugs in astronauts before, during, and after spaceflight: an observational study. *Lancet Neurol* 2014; published online August 8. [http://dx.doi.org/10.1016/S1474-4422\(14\)70122-X](http://dx.doi.org/10.1016/S1474-4422(14)70122-X).

## **Supplemental Materials**

Actigraphy and log data were collected for two weeks approximately three months before launch (Scheduled launch – 90 days; SL-90) and from eleven days prior to launch until launch day (L-11). Inflight, crewmembers donned the Actiwatch-L (AWL) as soon as possible upon entering orbit (STS) or when arriving on ISS (Soyuz-launched crewmembers) and doffed it before landing. Data were downloaded after the shuttle landed and monthly from the ISS. Participants were given an AWL as soon as possible after the landing and post-flight data were collected for one week (R+7).

Additionally, crewmembers were instructed to complete a daily sleep log within 15 minutes of awakening during all data collection intervals, with the exception of ISS flights where crewmembers were scheduled to complete the log for seven days approximately every three weeks. ISS crewmembers used a computerized version of the log allowing the option of declining participation in the question on medication use for the remainder of their mission. The sleep log contained subjective ratings of alertness and fatigue, subjective quantification of sleep, and documentation of sleep disturbances and medication usage.

For this study, we used the same data collection schedule that was previously negotiated with the operational management at NASA for sleep studies. Given the constraints on astronaut time, we were limited to collecting data for only one week after flight, and ISS crewmembers did not complete the sleep log on a daily basis.

Sleep duration was estimated in two-minute epochs from actigraphy data using Actiware Software (Version 3.4; MiniMitter/Phillips Respironics, Bend, OR). We used the actiwatch light data (which provided information about lights on and lights off) and incorporated the information that we had about the astronauts' schedules, with a visual inspection of each day of

data and manually set the analysis interval (or intervals, if naps occurred), rather than relying on an automated program that would include zero epochs as sleep. To aid us in interpreting the actigraphy data, crewmembers were instructed to note on the sleep log anytime they removed the actigraph or took a nap.

At the end of the SL-90 data collection and following the R+7 data collection, crewmembers were scheduled for 30-minute debriefs with investigators. Data were shared with the crewmember and a structured interview format was used to elicit additional information on his or her sleep. This included the opportunity to ask crewmembers about any ambiguities seen in the actigraphy data.

Within that manually established analysis window, we used the algorithm to set the start sleep and end sleep times and calculate the sleep and wake designations, including total sleep time. A modified sleep efficiency was calculated as total sleep time divided by the time between actigraph-defined start sleep and end sleep times. Subjective sleep quality and alertness were measured on the 100 mm non-numeric visual analog scales contained in the sleep log, anchored by poorly (0) and great (100) and sleepy (0) and alert (100), respectively. Crewmembers also reported lights out and lights on times (time in bed), the amount of time it took them to fall asleep (sleep latency) and their subjective estimate of sleep duration. The number of days on which sleep medication was taken and the reasons for sleep disturbances were tabulated from the sleep log.

In this report, crewmember refers to a member of a specific mission. An astronaut or participant refers to an individual and may be a member of multiple crews.

## **RESULTS/DISCUSSION**

Due to launch delays, planned travel or other operational contingencies, shuttle crewmembers' SL-90 data collection began, on average,  $124.0 \pm 59.2$  days prior to launch. For ISS crewmembers, SL-90 began, on average,  $130.4 \pm 59.2$  days prior to launch. Average shuttle mission duration was  $13.4 \pm 1.5$  days. Average ISS mission duration was  $155 \pm 39$  days.

Figure S1 shows the sleep conditions on shuttle (S1a) and ISS missions (S1b). Figures s2 and s3 illustrate the raw actigraphy data collected during L-11 and during a shuttle mission, respectively.

Average sleep duration among shuttle missions varied widely. Of the 26 shuttle missions, 22 had 2 or more crewmembers participate. Of those missions, average nightly sleep duration per mission ranged from 5.1 hours to 6.3 hours.

There was no trend in sleep duration over the course of the shuttle (Figure s4a) and ISS (Figure S4b) missions.

Twelve ISS crewmembers performed 34 EVAs and actigraphy data were available on 29 of the nights prior to EVA. On 24% (7/29) of nights before accomplishing EVAs, ISS crewmembers slept fewer than 6 hours; on 72% (21/29) of nights ISS crewmembers obtained less than 7 hours of sleep. No crewmember slept eight hours or more on the night before an EVA.

*Wakefulness-promoting countermeasures* Caffeine was widely used throughout all data collection intervals by both shuttle and ISS crewmembers, though supply shortages sometimes led to coffee rationing and reduced consumption aboard ISS<sup>s1</sup>. All but eight shuttle mission-crewmembers (72/80, 90%) and all but one ISS crewmember (20/21, 95%) reported using caffeine at least once during the study. During SL-90, 90% of shuttle mission crewmembers (72/80) and 95% of ISS crewmembers (20/21) reported using caffeine at least one day, 64%

(51/80) and 67% (14/21) reported using it every day, respectfully. Eighty-four percent of shuttle mission-crewmembers (66/79) and 95% of ISS crewmembers (20/21) reported caffeine use at least once during L-11, 67% (53/79) and 76% (16/21) reporting it daily. Seventy-nine percent of shuttle mission-crewmembers (65/77) and 95% of ISS crewmembers (19/20) reported caffeine use at least once inflight, 37% (29/78) and 38% (8/21) reporting it every day. During R+7, 84% of shuttle mission-crewmembers (65/77) and 95% of ISS crewmembers (19/20) reported using caffeine at least once, and 55% (42/77) and 50% (10/20) reported it every day.

Given the 3-7 hour half-life of caffeine and the sleep disturbances associated with its use<sup>s2</sup>, caffeine may have contributed to or enabled the sleep curtailment observed in this population. However, there is no evidence that caffeine accounts for the reduced sleep duration observed during spaceflight, as caffeine consumption was, if anything, reduced during spaceflight.

The wakefulness-promoting medication, modafinil, was reportedly used on both shuttle (10 reported uses) and ISS missions (2 reported uses). The use of this wakefulness-promoting medication was reported more frequently in post-flight debriefs.

We compared sleep data between shuttle missions and the first three weeks of ISS missions. There were no significant differences in the subjective or objective measures of sleep (Table s1) during these comparable time frames.

*Sleep disturbances.* On the daily log, shuttle crewmembers reported sleep disturbance on 701 (68%) of nights during the SL-90 interval, on 564 (68%) of nights during the L-11, on 534 (58%) of nights inflight, and on 360 (72%) of nights during the R+7 data collection interval. Voids were the most commonly cited reason for sleep disturbance during all data collection intervals (Table s2).

On the daily log, ISS crewmembers reported sleep disturbance on 144 (62%) of nights during SL-90 interval, on 130 (67%) of nights during the L-11 interval, on 349 (35%) of nights inflight, and on 78 (58%) of nights during the R+7 data collection interval. Similar to shuttle crewmembers, voids were the most commonly cited reason for sleep disturbance during all data collection intervals. (Table s3)

Because the shuttle missions were of a limited duration and tasks often time critical, crewmembers reported the need to stay up late to prepare for the next day's work activities (i.e., mission duties) more than three times as often inflight than during the SL-90 interval. ISS crewmembers reported their sleep was disturbed by mission duties twice as often inflight as during the SL-90 interval. As such, NASA is advocating research on inflight workload to determine the acceptable amount of work that should be permitted.<sup>s3</sup>

Another environmental factor, noise, which can disrupt slow wave and REM sleep, both of which are critical to the restorative function of sleep, remains a major source of sleep disruption in modern spaceflight. Both shuttle and ISS crewmembers attributed 1 in 5 inflight disruptions to noise. Disruption attributed to physical discomfort and other crewmembers was reduced by 31% and 76% on ISS compared to STS missions, respectively, likely attributable to the private sleeping quarters afforded ISS crewmembers. Planners of exploration class space missions should prioritize optimizing the environmental conditions of the spacecraft to reduce sleep disruptions on future missions.

Nocturnal micturition is common in this age group and was the most reported reason for disruptive sleep both on Earth and inflight. The percentage of disturbances attributed to a full bladder was less during spaceflight. This difference may be due to the choice of some crewmembers to wear maximum absorbency garments at night so that other crewmembers are

not disrupted by the noise associated with using the bathroom. Some crewmembers also reported reducing their fluid intake prior to bedtime to reduce the need to void during the sleep episode. Whether the need to urinate actually causes a given awakening cannot be determined from such attributional reports.

There are numerous other stressors that are unique to the spaceflight environment that might also account for sleep disturbances and prompt use of sleep-promoting medications. Further research might use this extensive sleep database to search for correlations between environmental factors that NASA routinely records (e.g., hypercapnia, noise) and sleep.

Furthermore, crewmembers experience 90-minute light/dark cycles during spaceflight. The brightest lighting is on the flight deck of the shuttle and in the cupola on the ISS. With direct sun exposure, light exposure in those locations can exceed 80,000 lux. On a previous shuttle mission, STS-90, the highest value observed in the middeck was 93 lux<sup>s4</sup>. The minimum limit allowable for the ISS is 108 lux as measured at 30 inches from the floor in the horizontal plane.<sup>s5</sup> Additional research should explore these highly variable lighting patterns and their effect on circadian rhythmicity and sleep.

## References

- S1. Stuster J. Behavioral issues associated with long-duration space expeditions: review and analysis of astronaut journals. NASA/TM-2010-216130. 2010. Houston, TX, Johnson Space Center.
- S2. Gillin J, Drummond S. Medication and substance abuse. In: Kryger MH, Roth T, Dement WC, editors. Principles and Practice of Sleep Medicine. Philadelphia: W.B. Saunders Company, 2000: 1176-1195.

- S3. Human health and performance risks of space exploration missions. McPhee J, Charles J, editors. SP-2009-3405. 2009. National Aeronautics and Space Administration.
- S4. (Dijk DJ, Neri DF, Wyatt JK, Ronda JM, Riel E, Ritz-De Cecco A, Hughes RJ, Elliott AR, Prisk GK, West JB, Czeisler CA. Sleep, performance, circadian rhythms, and light-dark cycles during two space shuttle flights. *Am J Physiol Regul Integr Comp Physiol*. 2001 Nov; 281(5):R1647-64.)
- S5. (ISS Flight Crew Integration Standard NASA-STD-3000/T, Rev E, Section 8.13, pages 11-16)

Figure S1. The STS-112 crew in their sleep restraints on the orbiter Atlantis middeck. (a). ISS crewmembers use sleeping bags in a private sleep chamber (b). Images provided by NASA.

Figure S2. Raw actigraphy data for one crewmember during L-11 data collection interval. Data are double plotted with black representing activity and yellow representing light. These data illustrate an initial phase delay in the crewmember's schedule (A). When the Shuttle launch was delayed, the crewmember flew back to Houston (B). The Shuttle launch was rescheduled and a phase advance schedule was initiated to meet the new launch time (C).

Figure S3. Two examples of inflight actigraphy data from two Shuttle crewmembers. Data are double plotted with black representing activity and yellow representing light. These data illustrate individual differences seen in sleep duration and quality. The crewmember on the left (A) mostly slept well. The crewmember on the right (B) had profoundly disturbed sleep.

EVA=Actigraph was off during EVA. X= Actigraph not worn during night.



Figure S4. Mean total sleep time measured via actigraphy (blue) with 95% confidence intervals (green) are shown across the duration of shuttle (a) and ISS (b) missions.

Figure s5. Each row represents a crewmember on one Space Shuttle mission. Each column represents the completion of one sleep log. No medication was reported in gray blocks, one dose of medication was reported in blue blocks and two doses of medication in red blocks.

**Table s1. Comparision of sleep outcomes between shuttle mission and first three weeks of ISS missions.**

	Inflight STS(Mean/SD) ISS(Mean/SD)	P STS vs. ISS
Time in Bed (Diary) (hours)	7·35/0·47 7·90/2·31	0.6026
Sleep Episode Time (Actigraphy) (hours)	6·73/0·46 6·65/0·79	0.1126
Total Sleep Time (Diary) (hours)	6·32/0·53 6·37/0·66	0.1856
Total Sleep Time (Actigraphy) (hours)	5·96/0·56 5·97/0·71	0.8371
Sleep Latency (Diary) (mins) *	23·63/14·75 13·94/12·95	0.0948
Sleep Quality (Diary)	63·70/13·35 68·89/17·14	0.2296

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Alertness	64·92/13·51	0.1032
(Diary)	58·18/25.06	

\*SL>240 minutes were excluded.

**Table s2.Space Shuttle crewmembers' reported causes of sleep disturbances**

<sup>a</sup> Crewmember could report more than one reason for disturbance

Most common reported causes of sleep disturbance	Number (Percentage) of disturbed nights <sup>a</sup>				
	<u>L-90</u>	<u>L-11</u>	<u>Inflight</u>	<u>R+7</u>	p
Voids	451(64·3)	447 (79·3)	131 (24·5)	259(71·9)	<0·0001
Noise	124(17·7)	76(13·5)	112(21·0)	45(12·5)	0·0010
Too cold	10(1·4)	9(1·6)	85(15·9)	8(2·2)	<0·0001
Other crewmembers	0 (0)	0 (0)	67 (12·6)	0 (0)	<0·0001
Too hot	46 (6·6)	34 (6·0)	56 (10·5)	30 (8·3)	0·0228
Mission duties	10 (1·4)	19 (3·4)	31 (5·8)	3 (0·8)	<0·0001
Physical discomfort	56 (8·0)	29 (5·1)	86 (16·1)	29 (8·1)	<0·0001

**Table s3. ISS crewmembers' reported causes of sleep disturbances**

<sup>a</sup> Crewmember could report more than one reason for disturbance

Most common reported causes of sleep disturbance	Percentage of disturbed nights <sup>a</sup>				
	<u>L-90</u>	<u>L-11</u>	<u>Inflight</u>	<u>R+7</u>	p
Voids	79 (54·9)	89 (68·5)	89 (25·5)	39 (50·0)	<0·0001
Noise	30 (20·8)	17 (13·1)	83 (23·8)	8 (10·3)	0·0081
Too cold	6 (4·2)	2 (1·5)	19 (5·4)	0 (0·0)	0·0593
Other crewmembers	0 (0·0)	0 (0·0)	11 (3·2)	0 (0·0)	0·0103
Too hot	8 (5·6)	4 (3·1)	65 (18·6)	4 (5·1)	<0·0001
Mission duties	8 (5·6)	12 (9·2)	32 (9·2)	4 (5·1)	0·3974
Physical discomfort	14 (9·7)	3 (2·3)	38 (10·9)	27 (34·6)	<0·0001

## Supplement-Sleep in Space



Figure S1a.



Figure S1b.

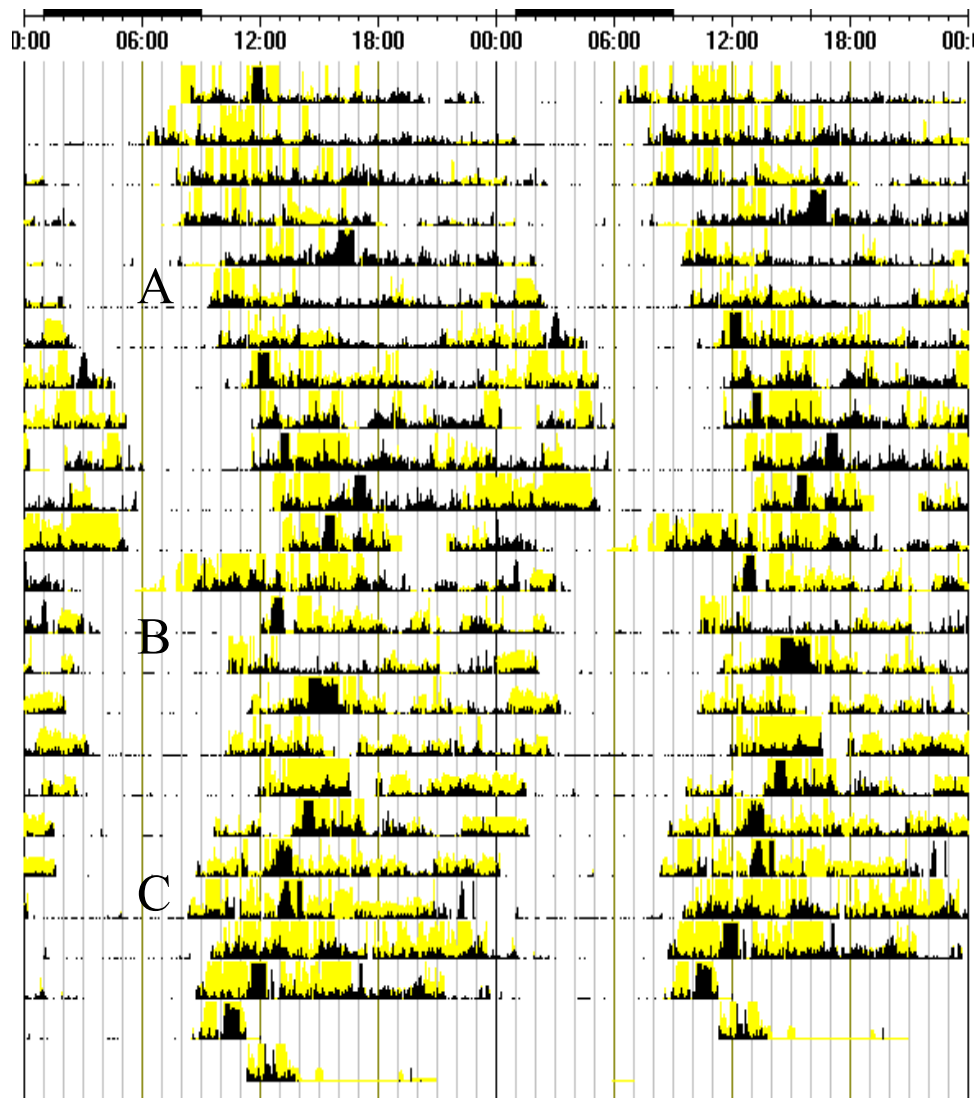
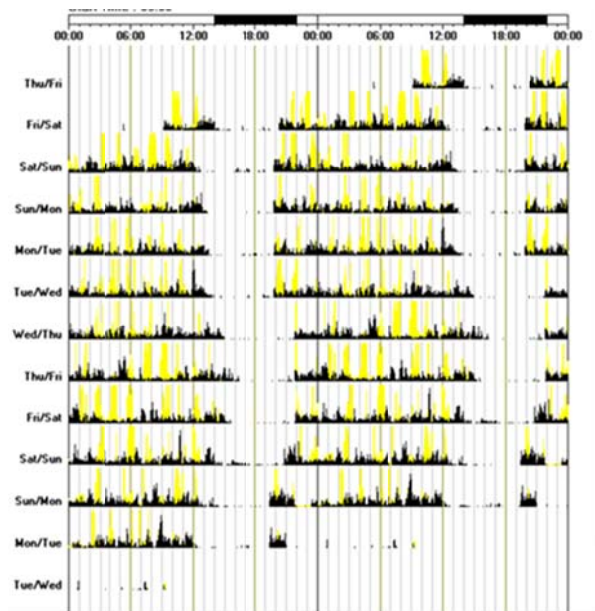


Figure S2.

## Supplement-Sleep in Space

A



B

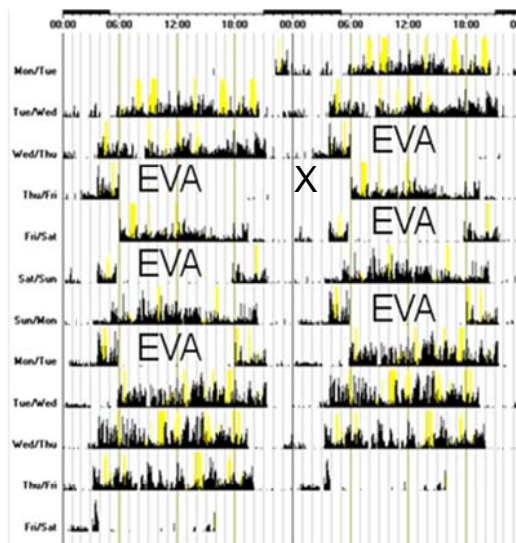


Figure S3.

## Supplement-Sleep in Space

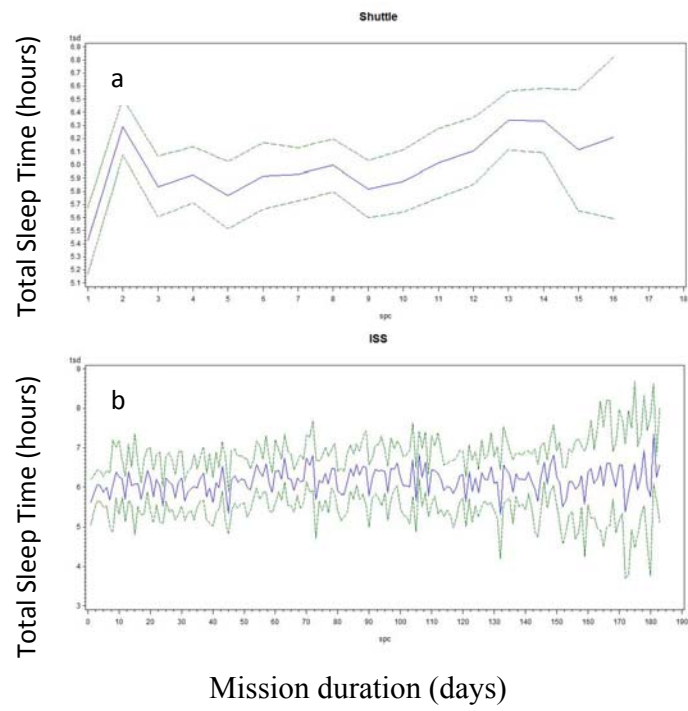


Figure S4.

Supplement-Sleep in Space

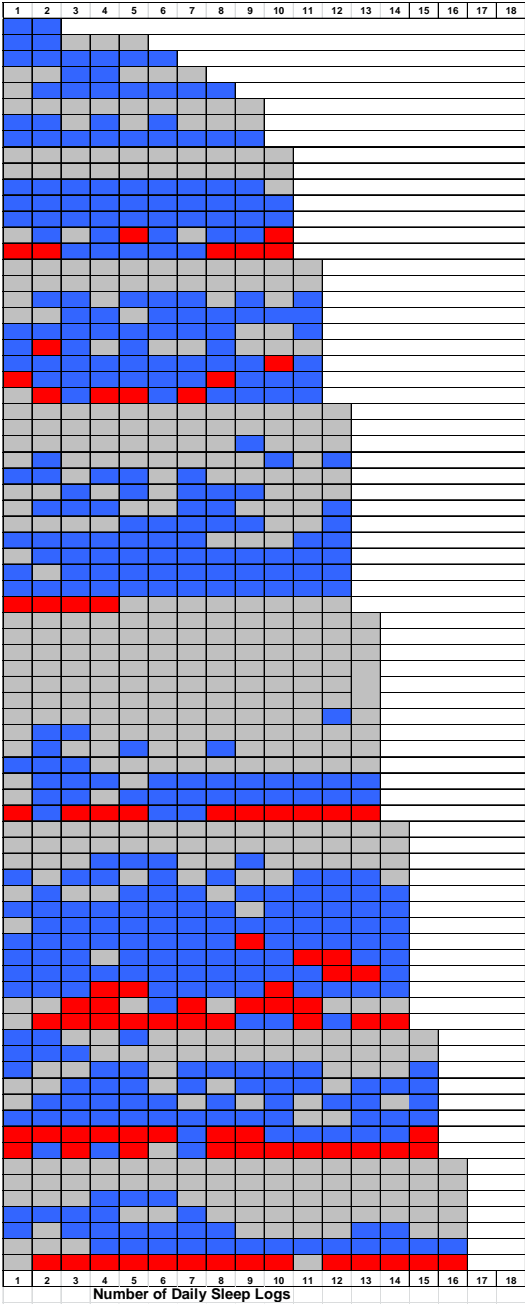


Figure S5.